REMARKS

Claim 12 has been canceled because it has come to applicant's attention that this claim is inconsistent with the method set forth in claim 1. Claim 1 is directed to a fluorescence assay where a light-emitting moiety is inhibited from such light emission by physical interaction with an indicator that is in the reaction mixture in proportion to the concentration of analyte. The sole outstanding rejection is based on asserted anticipation by Morris which, applicant will further explain below, discloses and refers to fluorescence assays where there is no physical interaction between the light-emitting moiety and a light-absorbing moiety which would be the counterpart of the indicator of the present invention.

In a further effort to explain this distinction, applicant submits, attached to the present submission, a copy of an article entitled "Quenching of Fluorescence" from the book Principles of Fluorescence Spectroscopy, 2nd Ed. (1999) Kluwer Academic/Plenum Publishers, New York, NY. The article is lengthy and need not be read in its entirety. On page 237, the article describes three types of quenching:

1. Collisional or dynamic quenching;
2. Static quenching; and
3. Apparent quenching.

The article states apparent quenching occurs due to the optical properties of the sample whereas dynamic and static quenching require direct physical interaction between the fluorescence-emitting moiety and the quencher. In apparent quenching, light is emitted but then absorbed; in dynamic or static quenching, no light is emitted all.

As noted on page 242, the previous section (dynamic or collisional quenching) describes quenching that results from diffusive encounters between the fluorophore and quencher during the lifetime of the excited state. The text goes on to say that quenching (static) can also occur as a result of the formation of a non-fluorescent complex between the fluorophore and quencher. When the complex absorbs light, it immediately returns to the ground state without emission of a photon. (See underlined portion.)

These types of quenching, thus, require molecular contact between with fluorescer and the quencher. See left-hand column page 237. No light is ever emitted.

But there is another type of fluorescence quenching that does not require physical interaction. In this case, light is emitted by the light-emitting moiety (emission is not inhibited as required by the claims) and simply absorbed by another component at a distance. This is apparent quenching, the type of quenching described by Morris.

The Office points to Morris, column 2, beginning at line 53, which cites a number of documents all of which, according to the end of the paragraph in column 3, describe "a synthetic substrate containing a quenching group and a fluorescing group which is generated to detect the activity of an enzyme." This is described in the enclosed "Quenching of Fluorescence" article on page 257, under the heading "Intramolecular Quenching." As described, the fluorescer and quencher are placed in proximity on a single molecule and held so that the emitted light from the fluorescer can be absorbed by the quencher. As they are covalently linked to each end of the peptide at a specific distance, they cannot diffuse to collide during the lifetime of the excited state of the fluorophore as it the case in collisional or dynamic quenching or form a complex as in static quenching.

That the Morris document itself does not involve direct physical interaction between the fluorophore and the quencher is made apparent by the section cited by the Office in column 4. Morris positions a fluorophore in a chemically inert light-transparent matrix to intersect the light path and detects the change in apparent emission of the fluorophore which is affected by the absorption qualities of the remainder of the reaction mixture. The fluorescer is not, and cannot be, in physical contact with the assay solution containing the indicator or chromophore, as is shown in Figure 1A. There cannot possibly be a physical interaction which inhibits the ability of the fluorescer to emit light.

By way of further explanation, applicant acknowledges that the bulk of the present application concerns the type of fluorescence quenching that is described by Morris. Indeed, the two exemplified protocols are based on this.[1]

Confusion was further caused by retention of claim 12 until its cancellation in this Office action since a light-absorbing moiety would be appropriate only for the apparent quenching described in the attached article, not the collisional/static quenching that requires direct physical interaction required by the claims.

Nevertheless, it should be noted that the specification is quite direct in making this distinction in paragraph 10. The application states that one mechanism included in the invention is that the light actually emitted may simply be absorbed. The stated alternative mechanism, also included in the invention and now claimed, is that there may be a physical interaction between the

[1] In the determination of glucose set forth in Table 3, the actual mechanism may be the interaction of hydrogen peroxide with the fluorescer, NBD. Hydrogen peroxide is an acknowledged participant in dynamic or collisional quenching as set forth in the attached article on page 239, bottom of the left-hand column. Since no detectable color of the oxidized O-dianisidine is generated, it is not clear that the yellow oxidized O dianisidine is formed at all, and the hydrogen peroxide may be interacting directly with the NBD.

"emitting" moiety and indicator such that the emission of fluorescence is inhibited. Thus, in the present claims, the fluorescence is not emitted at all when the collision occurs. In the case of the Morris-type quenching, emission occurs, but absorption is achieved at a distance.

Applicant notes that it is the Examiner's position that Morris clearly teaches fluorescence quenching which "encompasses the indicator physically and interacts with the light-emitting moiety." Applicant contests this for the reasons set forth above. The disclosure of Morris is confined to apparent quenching where light is actually admitted and then absorbed. This is clearly the case for the Morris invention itself and it is also the case for the prior art cited by Morris.

The Office goes on to note that the present claims do not contact anything but merely have the two steps of providing and determining and there is no contacting or reacting or correlating as are standard method steps.

Applicant takes this to mean that the Office expects that if there is a physical interaction between the fluorescer and the quencher, the claim should include a step whereby the performer of the assay takes two separate solutions and mixes them together. But that is not the point. The physical interaction is controlled simply by the diffusion of the molecules already contained in the assay solution, as is made clear by the attached document.

Applicant hopes that the distinction between collisional/dynamic/static quenching which require physical interaction between the fluorescer and quencher and prevents the light being emitted from the fluorescer in the first place, has been clearly distinguished from apparent quenching where the fluorescer emits light, but the absorber, at a distance, absorbs it so that it is not visible to the observer. Based on this distinction, Morris does not anticipate the invention as claimed.

Reconsideration in light of the foregoing discussion and amendment is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petitions for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 527832000420.

Respectfully submitted,

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